

REMARKS**Specification Amendment**

The paragraph at page 5, lines 1 through 10 has been amended to replace the expression “recognition fragment” with “restriction fragment” to correct a typographical error.

This amendment introduces no new matter.

Claim Amendments

Claims 1-31 have been cancelled. New Claims 32 – 51 have been added.

Support for Claim 32 is found, for example, on page 2, line 27 through page 3, line 3 and page 3, lines 22-24 of the specification as filed.

Claims 33 - 35 are drawn to the subject matter of Claims 3, 4 and 6, respectively, as originally filed.

Support for Claim 36 is found, for example, on page 3, lines 4-6 of the specification and on FIG. 4 as originally filed.

Support for Claim 37 is found, for example, on page 9, lines 21-25 of the specification as originally filed.

Support for Claim 38 is found, for example, on page 15, lines 13-19 of the specification as originally filed.

Claims 39 and 40 are drawn to the subject matter of Claims 10 and 11, respectively, as originally filed.

Support for Claim 41 is found, for example, on page 3, lines 17 – 25 of the specification as filed.

Support for Claim 42 is found, for example, in original Claim 1 and on page 3, lines 26-27, page 3, line 27, page 10, lines 1-9 and page 22, line 24.

Claim 43 is drawn to the subject matter of Claim 6, Claim 44 is drawn to the subject matter of Claim 2, and Claim 45 is drawn to the subject matter of Claims 3 and 4 as originally filed.

Support for Claim 46 is found, for example, on page 2, line 27 through page 3, line 3 and on page 3, lines 22-24 of the specification as filed.

Claims 49 and 50 are drawn to the subject matter of Claims 10 and 11, respectively, as originally filed.

Support for Claim 51 is found, for example, on page 3, lines 17 – 25 of the specification as filed.

These amendments introduce no new matter.

Substitute Sequence Listing

Applicants are submitting Substitute Sequence Listing concurrently herewith to correct an inadvertent error. Specifically, SEQ ID NO: 5 was shown in reverse orientation in the Sequence Listing previously filed.

This amendment introduces no new matter.

Rejection of Claims 1-6 and 8-12 under 35 U.S.C. §112, First Paragraph

Claims 1-6 and 8-12 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that is allegedly not adequately described in the disclosure in a way that conveys to one skilled in the art that the applicant possessed the claimed invention at the time the application was filed. The Examiner states that the number of possible nucleic acid sequences is very large and that the vectors are of any origin and can infect cells of any type. The Examiner's position is that the disclosure does not provide a representative number of examples to demonstrate that the claimed invention possessed the alleged utility and that the applicant had possession of the full scope of the claimed invention.

Applicants respectfully disagree. Where, as here (1) the inventive portion of the subject matter is disclosed and (2) any additional variability within the genus arises due to additional elements that are not part of the inventor's contribution, and when the level of knowledge and skill in the art would allow one skilled in the art to recognize that the applicant was in possession of the genus, the written description cannot be deemed defective. (See Written Description Guidelines Training Materials available at,

<http://www.uspto.gov/web/offices/pac/writtendesc.pdf>,
released March 1, 2000, Example 8, page 35.)

Here, Applicants' invention relates to the creation of a vector containing a nucleotide sequence encoding an snRNA, which sequence has been modified to allow for excision of a restriction fragment and insertion of a nucleotide sequence complementary to a predetermined sequence. This vector allows switching of target specificity of snRNAs with ease. The selection of appropriate vectors and restriction enzymes for use in the invention as claimed is well within the skill in the art, and it will be appreciated that such selection is based in part on the particular use. However, this selection in no way lessens the disclosure relating to the inventive concept of the application, and Applicants are not required to disclose that which is known in the art. Therefore, a skilled practitioner must conclude that the inventors had possession of the claimed invention at the time the application was filed.

Reconsideration and withdrawal of rejection are respectfully requested.

Rejection of Claims 1, 2 and 4 Under 35 U.S.C. §102 (b) over Tuschl *et al.*

Claims 1, 2 and 4 are rejected under 35 U.S.C. § 102 (b) over Tuschl *et al.*, EMBO 17(9): 2636-2650 (1998). The Examiner states that Tuschl *et al.* discloses a recombinant vector encoding U2 and U6 snRNA with a 40-nucleotide insertion cassette contained between two insertion sites.

Applicants submit that new Claims 32-51 are novel over Tuschl *et al.* because Tuschl *et al.* neither teaches nor suggests all the elements of the claimed invention.

New independent Claim 32 is directed to a vector comprising an isolated nucleotide sequence encoding a *single* snRNA modified so that a restriction fragment is excised and insertion sites are formed upon digestion with a restriction enzyme.

In pertinent parts (see, *e.g.*, Introduction, page 2637, right column and Material and Methods, page 2647, right column), Tuschl *et al.* discloses a vector comprising *both* U2 *and* U6 snRNA contained between two restriction sites of two different restriction enzymes, *StyI* and *BanI*. The vector contains a *randomly mutagenized* insertion cassette of 40 nucleotides in length. Thus, Tuschl *et al.* teaches a vector comprising *two* snRNAs.

New independent Claim 42 is directed to a vector comprising an snRNA coding sequence that includes *an insertion cassette* that contains a nucleotide sequence complementary to a *predetermined target*.

Vectors of Tuschl *et al.* contain partially randomized positions from large spans of U2 and U6 snRNA. These vectors formed a library of ribozymes of unknown properties and were screened for activity.

Unlike Tuschl *et al.*, the invention of Claim 42 is directed to a vector in which insertion of a cassette of a *pre-determined sequence* results in a vector that includes a nucleotide sequence complementary to a predetermined target. For instance, as exemplified in the application, a sequence directed against bases 1547-1556 of luciferase was cloned into the U1/Bae1 vector (page 22, line 24 of the specification).

Applicants submit that new independent Claims 32 and 42, as well as claims dependent thereon, are novel and not obvious in view of the teaching of Tuschl *et al.* because Tuschl *et al.* does not teach or suggest all the elements of the invention of Claims 32 and 42.

Reconsideration and withdrawal of rejection are respectfully requested.

Rejection of Claims 1-6, 8 Under 35 U.S.C. § 103 (a) Over Tuschl *et al.* in view of Cohen *et al.*

Claims 1-6 and 8 are rejected under 35 U.S.C. § 103 (a) over Tuschl *et al.*, EMBO 17(9): 2636-2650 (1998) in view of Cohen *et al.*, Proc. Natl. Acad. Sci. 91: 10470-10474 (1994).

Applicants submit that new Claims 32-51 are non-obvious over Tuschl *et al.* in view of Cohen *et al.*

Where the claimed invention is rejected as *prima facie* obvious in view of a combination of references, M.P.E.P. § 2142 requires that:

“[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.”

Reliance on the specification as filed for providing motivation to combine the two references impermissible. M.P.E.P. § 706.02 (j) recites:

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not be based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants submit that in view of the arguments presented above, Tuschl *et al.* does not teach all the elements of the claimed invention. Specifically, Tuschl *et al.* does not teach the elements of "single snRNA" of Claim 32 and an insertion cassette "wherein said insertion cassette comprises a modification fragment comprising a nucleotide sequence complementary to a predetermined target" of Claim 42. In pertinent parts (see Cohen *et al.*, Material and Methods) Cohen *et al.* teaches site-directed mutagenesis of a vector comprising a U1 snRNA. Applicants submit that the combination of Tuschl *et al.* and Cohen *et al.* does not render the claimed invention *prima facie* obvious.

Tuschl *et al.* expressly teaches away from using a single snRNA by teaching that snRNAs are not known to be catalytic in the absence of other spliceosomal components (Tuschl *et al.*, page 2637, right column, first full paragraph). Cohen *et al.* does not provide suggestion or motivation to use a recombinant vector comprising an isolated nucleotide sequence encoding a single snRNA, wherein said nucleotide sequence has been modified to contain one or more restriction sites, such that digestion with at least one restriction enzyme excises a restriction fragment and forms insertion sites in said nucleotide sequence, as required by Claim 32. Thus, one of ordinary skill in the art would not have been motivated to modify the teachings of the references or to combine the reference teachings to obtain the invention of Claim 32.

Moreover, neither Tuschl *et al.* nor Cohen *et al.* teach a recombinant vector comprising an isolated nucleotide sequence encoding an snRNA wherein said nucleotide sequence comprises an insertion cassette between two insertion sites, and wherein said insertion cassette comprises a modification fragment comprising a nucleotide sequence complementary to a predetermined target, as required by Claim 42. Thus, even if combined, Tuschl *et al.* and Cohen *et al.* do not teach all the elements of the invention of Claim 42.

Reconsideration and withdrawal of rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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